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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,062	02/21/2002	John David Charles Rosamund	056291-5073	8999

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,062	ROSAMUND ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *23 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 10 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed on 2/23/04 is acknowledged.

Status of Claims

2. Claim 2 is cancelled.

Claims 1 and 15 have been amended.

Claims 1, 10 and 15 are currently pending and are under examination.

Specification – Informalities Withdrawn

3. In view of amendment to the brief description of the drawing as set forth in 37 C.F.R.1.74, the specification of Informalities have been withdrawn.

Sequence Requirement Moot

4. In view of cancelation of SEQ.ID.NO: 12, 13, 14 and 15 in the specification on page 17, the sequence requirement is moot.

Claim Rejection - 35 USC 112 (written description) withdrawn

5. In view of amendment to claim 1, the rejection under 35 U.S.C. 112, first paragraph, written description rejection is withdrawn.

Claim Rejections - 35 USC 112, first paragraph maintained

6. The rejection of claims 1, 10 and 15 under 35 U.S.C. 112, first paragraph scope of enablement maintained as set forth in the previous office action.

The specification, while being enabling for a purified polypeptide having PMK activity comprising the amino acid sequence, SEQ. ID. NO: 7, a method to identify compounds that inhibit PMK activity of C.albicans, said method comprising contacting the test compound and the polypeptide SEQ.ID.NO: 7 and a diagnostic kit for detecting C.albicans comprising antibodies that specifically binding to the polypeptide SEQ.ID.NO: 7 does not reasonably provide enablement for (1) a purified peptide comprising a sequence possessing at least 90% identity, a method to identify compounds that inhibit phosphomevalonate kinase (PMK) activity comprising

contacting test compound with said sequence possessing at least 90% identity and (4) a diagnostic kit for detecting the presence of C.albicans comprising antibodies capable of binding to a sequence possessing at least 90% identity . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses an isolated polynucleotide sequence, phosphomevalonate kinase (PMK) that is described as ERG 8 gene from C.albicans and its encoding polypeptide, SEQ ID NO: 7. However, it fails to disclose a sequence possessing at least 90% identity to SEQ.ID.NO: 7. The instant claims comprising a sequence 90% identity are not predicted. The specification provides guidance and direction with regard to SEQ.ID.NO.7. However, there is no guidance or directions on how to make and how to use a polypeptide comprising a sequence 90% identity to SEQ.ID.NO: 7. It is known in the art that deletions, or modifications of the amino acids of a protein alter the function of the protein. The amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex (Bowie et al. Science, Vol. 247: 1990; p. 1306; p. 1308) and is well outside the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity/utility are limited in protein and the result of such modifications is unpredictable based on the instant disclosure.

The specification does not support the broad scope of the claims which encompass a nucleic acid molecule encodes a fragment which can be predictably modified and which regions are critical; what variants, if any, can be made which retain the biological activity of the intact protein; and the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful. Further, Houghten et al. (Vaccines, 1986, Edited by Fred Brown: Cold Spring Harbor Laboratory) teach that changes/modifications (addition, substitution, deletion or inversion) of one or more amino acids in a polypeptide will alter antigenic determinants and therefore affect antibody production (p. 21) as well as antibody binding. Houghten et al. also teach that "... combined effects of multiple changes in an antigenic determinant could result in a loss of [immunological] protection." And "a protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). Houghten et al. teach that point mutations at one key antigen residue could eliminate the ability of an antibody to recognize this altered antigen (p. 24). It is not always possible to make the derivatives that retain immunodominant regions and immunological activity if the regions have been altered. The specification teaches that specific primer or probes are required to amplify the PMK gene that encodes the polypeptide or its use in diagnostic for C.albicans. Therefore, any fragment or variant would not work in diagnostic kit for C.albicans or a method to identify compounds that inhibit PMK activity of the polypeptide.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed polypeptide i.e., fragment with 90% or in a diagnostic kit in a manner reasonably correlated with the scope of the claims broadly including any as presently claimed. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the protein renders activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins. However, even if it were shown that some modifications could be tolerated in the claimed peptide, for the reasons discussed the claims would still expectedly encompass significant changes, which could not be distinguished without undue experimentation. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Applicants' arguments filed on 2/23/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that claim 1 has been amended to cover polypeptides having PMK activity comprising the amino acid sequence depicted in SEQ.ID.NO: 7 and a sequence possessing at least 90%identity to SEQ.ID.NO: 7. Therefore, the invention no longer embraces any substitution, insertion or deletion resulting in at least 80% similarity to SEQ.ID.NO: 7, but rather includes only functional variants having a sequence that is at least 90%identical to SEQ.ID.NO: 7. Therefore, such variants may be used in diagnostic kits to identify compounds that inhibit PMK activity.

The examiner disagrees with the applicant for the following reasons: The claimed polypeptide comprises 432 amino acids. In order to obtain a sequence of 90% identity, roughly 43 amino acids have to be deleted or substituted or inserted. Therefore, to obtain a functional variant having a sequence that is at least 90%identical to SEQ.ID.NO: 7 is left for experimentation because the specification does not support the broad scope of the claims, which encompass modifications.

Applicant seems to agree with the examiner that mutation of a single amino acid may eliminate antigen recognition by a single antibody and yet states that many proteins exist that include substitution, mutation etc. Applicant states that the specification on pages 8 and 11 describe mutations may be introduced into a polynucleotide sequence by site directed mutagenesis and numerous ways to screen for PMK activity to make and use the claimed invention. It is the position of the examiner that while general methods of site directed mutagenesis and numerous ways to screen for PMK activity are known, the specification lacks support for a sequence that has 90% identity to SEQ.ID.NO: 7 that can be predictably modified and which regions are critical; what variant, if any, can be made which retain the biological activity of the intact protein and the specification provide essentially no guidance as to which screening assay for PMK is likely to be successful and which antibody recognizes this altered polypeptide and thus diagnose the presence of Candida albicans. Further, the claims 1 and 10 are not limited to ERG8 polypeptide from C.albicans having enzymatic activity. Further, claim 10 is not limited to the assays described in the specification because how a test compound inhibits the PMK activity of the claimed polypeptide in the absence of a substrate is not clear. It is concluded that the specification as filed is not enabling for the claimed invention as filed and an artisan would not have been able to practice the invention without undue experimentation. Therefore, limitation of the scope of the invention to an isolated and purified polypeptide from *C.albicans* having PMK activity comprising the amino acid sequence depicted in SEQ.ID.NO: 7 is proper.

Remarks

7. No claims are allowed.

set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

9. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.

5/3/04

LYNETTE R. F. SMITH
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